REMARKS

Claims 1, 14, 16 and 18 are pending in the instant application. Claims 1, 14, 16 and 18 have been rejected. Claims 16 and 18 have been canceled. Claim 1 has been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Non-Compliance of Previous Response

The Examiner suggests that the response filed September 1, 2005 is not compliant with the rules set forth under 37 C.F.R. §1.121, since the listing of claims does not show each and every change that has been made to claim 16 relative to the preceding version.

The comma replacing the period in claim 16 was an inadvertent typographical error. However, in light of the cancellation of claim 16 herein, correction of this error is moot.

II. Objection to the Specification

The specification has been objected to for failing to demarcate trademarks such as GenBank™ and Tween™. Applicant has amended the specification and therefore respectfully requests that this objection be withdrawn.

The specification also has been objected to for the impermissible referral to embedded hyperlinks and/or other forms of browser-executable code, and to the Internet contents so identified. Applicant has removed reference, at page 86, to the webpage index at the cancer.org website and therefore respectfully requests that this objection be withdrawn.

III. Non-Responsiveness of Rejection of Claims Under 35 U.S.C. 112

The Examiner suggests that the amendment filed on February 17, 2006 is non-responsive because entry of the amendment would amend all pending claims so as to be drawn to a patentably distinct invention, namely a method for reducing vascularization of a BMP-2 overexpressing tumor (*i.e.*, a lung tumor) in a subject comprising administering to a subject at risk of developing a tumor that overexpresses BMP-2 a therapeutically effective amount of an inhibitor of an activity of BMP-2. It is suggested that the invention of claim 1 and 14, as would be amended, is patentably distinct from the originally presented invention because the processes are materially different processes since each comprises administering the inhibitor to a distinct population of subjects (*i.e.*, either subjects having a tumor or subjects at risk for developing a tumor), wherein as amended, the claims would read on preventing the development of a tumor. The Examiner suggests that this is in contrast to the claims as originally filed, which were interpreted as a process for treating an established tumor in a subject. It is suggested that entry of the amendment would require the Examiner to perform a new search, make new considerations and raise new issues. Applicant respectfully disagrees.

As amended in the preliminary amendment filed March 9, 2005, claim 1 recited "A method of reducing vascularization of a tumor in a subject comprising administering to a subject a therapeutically effective amount of a bone morphogenetic protein-2 (BMP-2) activity inhibitor thereby reducing vascularization of

a tumor in the subject." In the broadest interpretation, this claim reads on inhibiting the vascularization of a new tumor as well as vascularization of an existing tumor. Accordingly, it is respectfully believed that amendment of claim 1 to read on preventing tumor vascularization is encompassed within the scope of the claim originally under examination. However, in an earnest effort to facilitate the prosecution of the present application, Applicant has amended claim 1 to recite administering a therapeutically effective amount of an inhibitor of an activity of BMP-2 to a subject in need of treatment. Support for this amendment is found in the claims as originally filed and amended on March 9, 2005.

Regarding the rejection of claims 1, 14, 16 and 18 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, Applicant's respectfully submit that, as amended, the instant claims meet the enablement requirement for the following reasons.

At the outset, Applicant respectfully disagrees with the Examiner's suggestion that a role for BMP-2 needs to be established before the therapeutic benefit of noggin can be realized. There is no such requirement for enablement. What is required is that the disclosure, when filed, contains sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art *to make and use* the claimed invention. MPEP 2164.01. In this regard, Applicant has established that a correlation exists between the overexpression of BMP-2 in a lung tumor and the use of a BMP-2 activity inhibitor such as noggin to reduce vascularization of such a lung tumor. Applicant's own publications published in 2003 and 2004

support this finding by showing that *in vivo* lung tumor growth is inhibited by BMP-2 antagonists. Accordingly, in an earnest effort to highlight this feature of the present invention, Applicant has amended the claims to indicate that the tumor being treated is a lung tumor. Support for this amendment is found throughout the specification and in particular in the Examples of the specification.

Moreover, in meeting the enablement requirement, Applicant has used a *bona fide in vivo* animal model for lung cancer and demonstrated that noggin reduces vascularization of lung tumors *in vivo*. The use of human A549 mouse xenografts for evaluating therapeutic efficacy of drugs for treating lung cancer is well-established in the art. For example, Sirotnak et al. ((2000) *Clin. Cancer Res.* 6:4885-92; abstract enclosed herewith) teach that co-administration of ZD1839 with cytotoxic agents is highly effective at regressing A549 tumors in mice. In phase I clinical trials with this same drug (*i.e.*, ZD1839), toxicity was manageable and clinical responses were observed in patients with various malignant tumors, in particular non-small cell lung cancer (see Meric et al. (2000) *Bull. Cancer.* 87(12):873-6; abstract enclosed herewith). Thus, Applicant has provided an *in vivo* animal model example in the specification, which one of skill in the art would readily recognize as a working example commensurate in scope with the amended claims. MPEP 2164.02 states that if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate.

The Examiner has provided no such evidence for the disclosed *in vivo* animal model. What has been provided is a general commentary on the use of *in vivo* mouse models (*e.g.*, Schuh, Bibby, Peterson), references pertaining to cancers other than lung cancer (*e.g.*, Hardwick, et al., Haramis, et al., Nishanian et al., Ghosh-Choudhury et al., Tomari et al., Nakamura et al., and Wen et al.), and *in vitro* results of BMP-2 suppression of A549 lung cancer cells (*e.g.*, Tada et al. and Buckley et al.). Unlike the teachings of Tada and Buckley, Applicant has placed lung tumor cells under the complex conditions of the *in vivo* environment, wherein the cells are subjected to various growth factors and cell-to-cell contact. Without this *in vivo* context, the teachings of Tada and Buckley can be held to contradict the instant results.

As shown in Figure 10, Applicant has demonstrated that by co-injecting noggin with lung cancer cells, lung tumor growth and vascularization can be reduced thereby providing benefit to a patient in need of treatment. Accordingly, the disclosed example exemplifies the use of the claimed method.

In an earnest effort to facilitate the prosecution of the claims 1 and 14, drawn to the use of noggin protein, Applicant is canceling claims 16 and 18, reserving the right to file continuing applications for the canceled subject matter.

Accordingly, given that Applicant has provided a disclosure which contains sufficient information regarding the subject matter of the claims and further provided a working example commensurate in scope with the claims, one skilled in the pertinent art could readily make and use the claimed invention.

It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

IV. Conclusion

The Applicant believes that the foregoing comprises a full and complete response to the Office Communication of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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